REMARKS

This responds to the Office Action mailed on June 16, 2005.

No claims are amended, added, or newly canceled; as a result, claims 1-58 and 60-63 are now pending in this application.

§112 Rejections of the Claims

1. Indefiniteness rejection

Claim 60 was again rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. This rejection is respectfully traversed.

The Examiner considers indefinite the phrase *condition treatable with stem cell transplantation, with or without gene therapy* because it is unclear to the Examiner, based on a reading of Applicant's specification, which conditions other than sickle cell anemia and lysosomal and peroxisomal storage diseases are so treatable. It is also unclear to the Examiner "when and if a condition encompassed by Applicant's invention requires gene therapy since it is unclear what conditions are of interest." Office Action at page 3.

Applicant submits that the Examiner has improperly isolated a phrase from the claim and analyzed that phrase for definiteness. A proper analysis of a claim must include the claim in its entirety and not bits and pieces of the claim taken out of context. Thus, an analysis of present claim 60 must include the verbiage that precedes and follows the phrase *condition treatable with stem cell transplantation, with or without gene therapy*. The phrase at issue therefore should be *treating a condition treatable with stem cell transplantation, with or without gene therapy, that utilizes bone marrow ablation.*

It is axiomatic that claim definiteness is not analyzed in a vacuum, but rather in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP § 2173.02 (emphasis added). The Examiner has restricted her analysis to the application disclosure and has failed to consider the teachings of the prior art and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. It is known in the art that bone

marrow ablation and stem cell transplantation are used together to treat hematologic cancer or genetic disorders, including storage disease, hemoglobinopathies, or severe immunodeficiency. See, for example, the web articles from www.oncolink.com and www.clinicaltrials.gov, and U.S. Patent 6,767,531 (for example, column 6, lines 24-39 and column 20, line 16 to column 21, line 15) copies of which are provided for the Examiner's convenience. Accordingly, one would have no difficulty in determining what conditions beyond those disclosed in Applicant's specification are encompassed by present claim 60.

The Examiner is under the impression that "claim 60 encompasses a vast number of possible conditions." Office Action at page 4 (in connection with the scope of enablement rejection). She has provided no evidence to support this statement. Applicant disagrees that hematologic cancer and genetic disorders are broad enough to encompass a vast number of possible conditions. The routineer would know exactly which of these disorders is amenable to treatment with a combination of bone marrow ablation and stem cell transplantation. However, even if these treatment options were considered broad, the Examiner is reminded that breadth is not to be equated with indefiniteness. MPEP § 2173.04. A rejection under the second paragraph of section 112 is inappropriate in such a situation.

Withdrawal of this rejection is respectfully requested.

2. Scope of enablement rejection

Claim 60 was rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for conditions treatable with stem cell transplantation, with or without gene therapy, that utilize bone marrow ablation such as sickle cell anemia and lysosomal and peroxisomal storage diseases, allegedly does not reasonably provide enablement for all conditions treatable with stem cell transplantation, with or without gene therapy. This rejection is respectfully traversed.

When rejecting a claim under the enablement requirement of section 112, the Examiner bears the "initial burden of setting forth a reasonable explanation as to why [he/she] believes that the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner bears the burden of providing evidence or technical

reasoning to substantiate her doubts that the specification is not enabling with respect to the scope of a claim sought to be patented. *Ibid. See also* MPEP § 2164.04. Without evidence or technical reasoning to doubt the truth of the statements made in the application, the application must be considered enabling. *Ibid.* In addition, an enablement rejection should be stated with a full development of the reasons rather than by a mere conclusion coupled with some stereotyped expression. MPEP § 706.03.

The Examiner has touched briefly on some of the *In re Wands* factors at pages 4 to 6 of the Office Action. However, the Examiner's conclusions appear to be doubts unsubstantiated by evidence or technical reasoning, and appear to be mere conclusions coupled with stereotyped expression, specifically proscribed by MPEP § 706.03. Thus, for example, under *3)Level of one of ordinary skill in the art* at page 4, the Examiner stated, "[d]ependent claim 60 encompasses a vast number of possible conditions." She made the same or similar statement under *5)Amount of direction and guidance provided by the inventor, 6)Existence of working examples*, and *7)Breadth of claims*. In addition, the Examiner has concluded that "[t]he art pertaining to the [sic] stem cell transplantation, with and without gene therapy is highly unpredictable." Office Action at page 5. All of these statements are unsubstantiated by evidence or technical reasoning. Further, as Applicant has established above with respect to the indefiniteness rejection by citation of documents, disorders amenable to treatment with a combination of bone marrow ablation and stem cell transplantation are known in the art. The number of these disorders is hardly vast, and nothing in the documents cited by Applicant is indicative of unpredictability in the art.

Therefore, the Examiner's rejection is based on a flawed and unsubstantiated premise, a premise which cannot survive in view of the knowledge of the person skilled in this art. The Examiner is reminded that without evidence or technical reasoning to doubt the truth of the statements made in the application, the application must be considered enabling. Applicants do not bear the burden of proving statements made in their application. The Examiner's mere gainsaying of Applicants' statements is not evidence or technical reasoning.

Allowable Subject Matter

Applicant acknowledges with the appreciation the allowability of claims 1-58 and 61-63.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6903 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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By his Representatives,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 3rd day of August, 2005.

Dawn M. Poole _____
Name

Dawn M. Poole
Signature

REUTERS

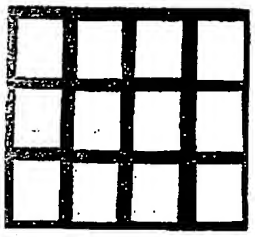
Last Updated: 2004-08-13 15:20:16 -0400 (Reuters Health)

NEW YORK (Reuters Health) - Hematopoietic stem cells can be modified to engraft within the host more efficiently, according to a new study, offering hope that cord blood transplants can someday be used to treat adults who must undergo bone marrow ablation for treatment of cancer or other major hematologic disorders.

"The problem with cord blood stem cell transplants is that the number of cell needed is directly proportional to the body weight of the patient," Dr. Hal E. Broxmeyer, senior author of a paper in the August 13th issue of Science, tolc Reuters Health. "Not all the stem cells that you put into the body traffic to where they need to be find the right environment and grow."

For that reason, umbilical cord blood transplants are not usually offered to adults, even though they offer a rich source of na□ve hematopoietic stem cells. Results of efforts to expand cord blood stem cells ex vivo prior to transplantation have "not been encouraging," Dr. Broxmeyer noted.

An alternative would be to treat hematopoietic stem cells to enhance their transplant efficiency. "We found that by manipulating a surface determinant stem cells, dipeptidylpeptidase IV (CD26), they not only home to bone marrc better, they engraft more efficiently," Dr. Broxmeyer said. "This was especial apparent when we used limiting numbers of cells," as is the case with cord blood transplants.



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Glimpses in a Window Series
by Patricia M. Siembora

The research team, based at the Indiana University School of Medicine in Indianapolis, took bone marrow cells from mice and treated them ex vivo wit either Diprotin A, a three-amino-acid peptide, or Val-Pyr, a two-amino-acid peptide, to inhibit CD26.

When injected intravenously, there was a 1.5-fold increase in short-term homing to recipient bone marrow compared with untreated cells. Using cells from CD26-/- knockout mice resulted in a 2.6-fold increase.

CD26-/- donor cells also made a significantly greater contribution than did control cells to peripheral blood leukocytes 6 months after transplant, indicating enhanced long-term engraftment, the authors report.

When lethally irradiated mice were injected intravenously with 25,000 norma stem cells, none lived beyond 21 days. When the same number of CD26-/- cells were injected, however, 80% survival was observed at day 60.

The peptides they used to inhibit CD26 do not seem to have adverse effects when used on animals, Dr. Broxmeyer added, so future studies will test thes inhibitors on human cells that will then be transplanted into immune-deficien mice to test their engraftment efficiency. Another mechanism of deleting CD from human cells may be gene transfer of short interfering RNA.

"But obviously there remains a lot of testing and controlled experiments in animals before we can start any clinical trials," he added.

Science 2004;305:1000-1003.

print article

Combination Chemotherapy Followed by Donor Bone Marrow Transplantation or Peripheral Stem Cell Transplantation in Treating Patients With Hematologic Cancer or Genetic Disorders

Sponsors and Collaborators: Herbert Irving Comprehensive Cancer Center
National Cancer Institute (NCI)

Information provided by: National Cancer Institute (NCI)

Purpose

RATIONALE: Peripheral stem cell transplantation or bone marrow transplantation may be able to replace immune cells that were destroyed by chemotherapy used to kill tumor cells.

PURPOSE: Phase II trial to study the effectiveness of combination chemotherapy followed by donor bone marrow transplantation or peripheral stem cell transplantation in treating patients who have hematologic cancer or genetic disorders.

Condition	Intervention	Phase
childhood Hodgkin's lymphoma childhood non-Hodgkin's lymphoma Leukemia Lymphoma plasma cell neoplasm	Drug: anti-thymocyte globulin Drug: cyclosporine Drug: fludarabine Drug: melphalan Drug: methylprednisolone Drug: mycophenolate mofetil Procedure: allogeneic bone marrow transplantation Procedure: biological response modifier therapy Procedure: bone marrow ablation with stem cell support Procedure: bone marrow transplantation Procedure: chemotherapy Procedure: graft versus host disease prophylaxis/therapy	Phase II

	Procedure: peripheral blood stem cell transplantation Procedure: supportive care/therapy Procedure: syngeneic bone marrow transplantation	

MedlinePlus related topics: Hodgkin's Disease; Leukemia, Adult Acute; Leukemia, Adult Chronic; Leukemia, Childhood; Lymphoma; Multiple Myeloma

Study Type: Interventional
Study Design: Treatment

Official Title: Phase II Study of Fludarabine and Melphalan Followed By Allogeneic or Syngeneic Bone Marrow or Peripheral Blood Stem Cell Transplantation in Patients With Hematologic Malignancies or Genetic Disorders

Further Study Details:

OBJECTIVES:

- Determine the hematopoietic recovery in patients with hematologic malignancies or genetic disorders treated with fludarabine and melphalan followed by allogeneic or syngeneic bone marrow or peripheral blood stem cell transplantation.
- Determine the chemotherapeutic toxicity of this regimen in these patients.
- Determine the relapse and survival of patients treated with this regimen.
- Determine the incidence of graft-versus-host disease in patients treated with this regimen.

OUTLINE: Patients receive fludarabine IV on days -6 to -2 and melphalan IV on days -3 and -2. Patients with a non-HLA-identical family member may also receive anti-thymocyte globulin on days -4 to -1. Patients undergo allogeneic or syngeneic bone marrow or peripheral blood stem cell transplantation on day 0. Patients receive graft-vs-host disease prophylaxis comprising mycophenolate mofetil twice daily beginning on day -3, methylprednisolone beginning on day 5 and continuing over 8 weeks, and cyclosporine IV or orally beginning on day -3 and continuing until at least 6 months post-transplantation.

Patients are followed at 1, 3, and 6 months, and then at 1 year post-transplantation.

PROJECTED ACCRUAL: A total of 52 patients will be accrued for this study within 5-6 years.

Eligibility

Ages Eligible for Study: 1 Year - 80 Years, Genders Eligible for Study: Both

Criteria

DISEASE CHARACTERISTICS:

- Clinically and/or histologically confirmed hematologic malignancy or genetic disorder
- Chronic myelogenous leukemia
- Typical blood and marrow morphology
- Presence of Philadelphia chromosome OR
- Molecular evidence of bcr/abl rearrangement if Philadelphia chromosome-negative
- Acute myeloid leukemia, acute lymphocytic leukemia, myelodysplasia, or lymphoma
- High risk of relapse or progressive disease
- Typical clinical features and morphology in blood, marrow, lymph node, or other tissue by cytochemistry, immunophenotyping, and/or chromosomal abnormalities
- Multiple myeloma
- Typical marrow morphology, radiographic findings, and paraprotein
- Aplastic anemia
- Typical marrow and blood findings
- Genetic disorder including storage disease (e.g., adrenoleukodystrophy), hemoglobinopathies (e.g., thalassemia), or severe immunodeficiency
- Unwilling to undergo conventional high-dose chemoradiotherapeutic conditioning prior to allogeneic stem cell transplantation OR
- Presence of other medical disorder which precludes high-dose chemoradiotherapeutic conditioning (e.g., cardiac disease or infection)
- Syngeneic twin, HLA-identical, or 1 or 2 HLA antigen-mismatched family member or unrelated donor

PATIENT CHARACTERISTICS: Age:

- 1 to 80

Performance status:

- Karnofsky 50-100%

Life expectancy:

- Not specified

Hematopoietic:

- Not specified

Hepatic:

- Not specified

Renal:

- Not specified

Other:

- No other serious medical or psychiatric illness that would preclude study compliance
- Not pregnant or nursing

PRIOR CONCURRENT THERAPY: Biologic therapy:

- See Disease Characteristics

Chemotherapy:

- See Disease Characteristics

Endocrine therapy:

- Not specified

Radiotherapy:

- See Disease Characteristics

Surgery:

- Not specified

Location and Contact Information

Please refer to this study by ClinicalTrials.gov identifier NCT00008307

New York

Herbert Irving Comprehensive Cancer Center at Columbia University, New York, New York, 10032, United States; Recruiting
David G. Savage, MD 212-305-9783

Study chairs or principal investigators

David G. Savage, MD, Study Chair, Herbert Irving Comprehensive Cancer Center

More Information

Clinical trial summary from the National Cancer Institute's PDQ® database

Study ID Numbers: CDR0000068396; CPMC-IRB-8462; CPMC-IRB-CAMP-25; NCI-G00-1897; NCT00008307
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Health Authority: United States: Federal Government
ClinicalTrials.gov processed this record on 2005-07-12